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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/765,458

01/27/2004

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BP-0207US

8587

23544 7590 09/03/2009
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EXAMINER

GAKH, YELENA G

ART UNIT

PAPER NUMBER

1797

MAIL DATE

DELIVERY MODE

09/03/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/765,458	Applicant(s) PAPPIN ET AL.	
	Examiner Yelena G. Gakh, Ph.D.	Art Unit 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 August 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 42-45 and 104-108 is/are pending in the application.
- 4a) Of the above claim(s) 42 and 106 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 43-45, 104, 105, 107 and 108 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Election of piperazine derivatives filed on 06/10/09 is acknowledged. Claims 42-45 and 104-108 are pending in the application. Claims 42 and 106 are withdrawn from consideration. Claims 43-45, 104-105 and 107-108 are considered on merits.

Specification

2. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
- (d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
- (e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
- (f) BACKGROUND OF THE INVENTION.
 - (1) Field of the Invention.
 - (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (g) BRIEF SUMMARY OF THE INVENTION.
- (h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
- (i) DETAILED DESCRIPTION OF THE INVENTION.
- (j) CLAIM OR CLAIMS (commencing on a separate sheet).
- (k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to as not containing a written description of the invention "in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same".

The specification is not arranged in the manner provided by the guidance, which ensures a clear and concise description of the invention, and in general is written in unclear and vague language in regards to the subject matter considered by the Applicants as inventive and non-obvious over the prior art. The specification does not contain a Summary of the Invention which allows understanding, as to what specifically the Applicants consider the essence of their invention. In combination with the vague and indefinite language of the claims, which recite "a method, comprising reacting two or more samples, comprising one or more reactive analytes, with a different labeling reagent" without specifying, as to what is the purpose of such method, the specification does not meet the requirements of the first paragraph of 35 U.S.C. 112. The description of the "Field of the Invention" as "analyte determination by mass analysis" is so general and broad, that it does not reflect to any extent the inventive subject matter. The only specific disclosure provided in the specification in regards to the claimed subject matter is related to specific examples, which therefore will be considered as the only enabling disclosure of the instant application. In other words, the only enabling disclosure is pertained to specific examples, which disclose proteomic analysis based on mass spectrometry of specifically labeled proteins with the labels provided in the examples and the proteins being extracted, digested and separated. Moreover, not all specific labels disclosed in the specification enable performing the method, since e.g. there is no experimental evidence for thiocarbonyl linker to be capable of providing the function required by the instant method, taking into account the reactivity of thiocarbonyl compounds (see page 50, lines 12-17).

The examiner will accept any changes in the specification, which will not introduce new matter to the disclosure, but which will help to clarify the essence of the invention.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 43-45, 104-105 and 107-108 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The examiner respectfully reminds the Applicants that according to MPEP §2163:

"2163.02. Standard for Determining Compliance with Written Description Requirement:

The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

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The claims recite a method comprising reacting two or more samples, comprising one or more reactive analytes with a different labeling agent. It is totally unapparent from the claim, what the method is directed to. The specification discloses analyte determination by mass spectrometry as the field of the invention. No analyte determination by mass spectrometry is claimed. Furthermore, the only analytes which were determined were peptides. No other analytes were disclosed in the specification as being determined with isobaric labels of the claimed method. Therefore, the Applicants did not reasonably convey to those skilled in the art that they "had possession at that time of the later claimed subject matter" in the scope of the claims.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 43-45, 104-105 and 107-108 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite a method of reacting two or more samples without any indication, as to what the method is directed to. This renders the claims unclear and indefinite, since it is not apparent from the claims, why this reacting should be performed. Furthermore, it is not clear, as to what might be the nature of the analyte, which also renders the claims unclear and indefinite.

Claim Rejections - 35 USC § 103

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. **Claims 43-45, 104-105 and 107-108** are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhou et al. (Nature Biotechnology, 2002, IDS) (Zhou) in view of Van Ness et al. (EP 0990047 B1, IDS) (Van Ness).

Zhou teaches "quantitative proteome analysis by solid-phase isotope tagging and mass spectrometry" (Title), comprising tandem LC-MS/MS spectrometry of at least two peptide samples tagged with isotopically enriched labels comprising different heavy atom isotopes and reporter moieties (see page 512 and Figure 1), which means that

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the at least two peptide samples are reacted with a labeling reagent comprising "a heavy atom isotope" and a reporter moiety,

tandem MS/MS analysis is performed, i.e. steps c) and d).

Internal standard is added to the mixture (see page 514, right column, first paragraph).

Zhou discloses reporter moieties being substituted aromatics, rather than substituted or non-substituted piperidine compound.

Van Ness discloses a method of detecting nucleic acids with mass spectrometry using labeling reagents comprising substituted aromatics, as well as substituted or non-substituted piperidine compound. The important feature of reporter moieties for both peptides and nucleic acids MS/MS detection is the presence of amino group, which makes reporter moieties disclosed by Van Ness suitable for Zhou's method.

Thus, it would have been obvious for a person of ordinary skill in the art to substitute aromatic reporter moiety in Zhou's method with any of substituted or non-substituted piperidine reporter disclosed by Van Ness, because they all have the same functional groups, which are essential for creating labels in MS/MS analysis of peptides and nucleic acids.

Double Patenting

10. Claims 43-45, 104-105 and 107-108 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 38-43 of copending Application No. 10/765,264. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Y. Kim can be reached on (571) 272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Yelena G. Gakh/
Primary Examiner, Art Unit 1797

8/28/2009